

## REVIEW

# Is there a critical period for bone response to weight-bearing exercise in children and adolescents? a systematic review

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This systematic review examines and compares the bone mineral changes in children and adolescents, as measured by dual energy x ray absorptiometry, reported in exercise intervention studies. The effects of hormonal factors and growth on bone mineral change during puberty are examined, and the possibility of a critical period during which bone is especially adaptable to exercise is discussed.

during this time may pose a risk for low adult bone mass. However, even "normal" accrual may not lessen the incidence of osteoporosis, as the incidence of osteoporotic fracture is increasing in the ageing population.<sup>8</sup> Thus, intervention strategies, implemented across the ages, may be necessary to promote lifetime bone health and bone strength. It is possible that the greatest opportunity for influencing bone mineral accrual lies in modifying physical activity during the growing years.

Several exercise interventions in children have shown a greater bone mineral change in exercising children over a relatively short (7–9 months) time compared with respective controls.<sup>1–6</sup> In general, the femoral neck and lumbar spine were most often positively affected by loading exercise. A large increase (in time and/or impact) of exercise in prepuberty elicited greater bone mineral gains at a range of skeletal sites compared with controls,<sup>2,4</sup> whereas less intensive exercise programmes have also shown a positive response at the trochanter, femoral neck, and lumbar spine in late prepubertal and early pubertal children.<sup>3,6</sup>

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Implementation of exercise interventions concurrently within distinct maturity groups provides evidence of a "window of opportunity" for bone response in early puberty.<sup>5,6</sup> Further work in a range of maturity groups in girls and boys will clarify the potential for loading induced osteogenesis across childhood and into puberty. There is an urgent need for longer intervention periods to determine if gains continue beyond 10 months, or if they reach a plateau. Short (2–3 year) and long (5–10 year) follow ups will also be needed to determine whether gains are maintained in the longer term or whether the interventions merely accelerate the achievement of a predetermined bone mass.

Children gain as much bone in the two years around the pubertal growth spurt as they will lose after their adult peak has been reached.<sup>7</sup> The time of transition from childhood to adolescence is critical to healthy bone mineral accrual, and interruptions in the normal pattern of bone gain

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Evidence suggests that weight-bearing physical activity during childhood has a positive, and possibly enduring, effect on variables related to bone strength.<sup>9–13</sup> In prepubertal and peripubertal children, the results of longitudinal<sup>14,15</sup> and intervention studies<sup>1–5</sup> support the notion that increased activity stimulates bone mineral accrual. However, probably because of variations in the interventions, and in the sex and maturity of the study groups, the bone response to loading interventions has varied in magnitude and by skeletal region.

The idea of a window of opportunity when bone is most responsive to exercise is an attractive possibility, worthy of our resources as investigators and attention as clinicians. This is because, given the currently low physical activity levels of many children,<sup>16</sup> and the general lack of interest in physical education in elementary schools,<sup>17</sup> it may be impossible to implement publicly funded exercise programmes to enhance bone mineral accrual to benefit children at every age. Ideally, exercise should be promoted at all ages for a range of health benefits.

Late childhood through early adolescence represents a time when biological factors associated with bone growth and development vary considerably depending on a child's level of maturity. This is further complicated by the rapid biological changes we observe during growth within a relatively short time frame. In this review, we briefly examine endocrine changes

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Abbreviations: DEXA, dual energy x ray absorptiometry; BMD, bone mineral density; BMC, bone mineral content; IGF, insulin-like growth factor; GH, growth hormone

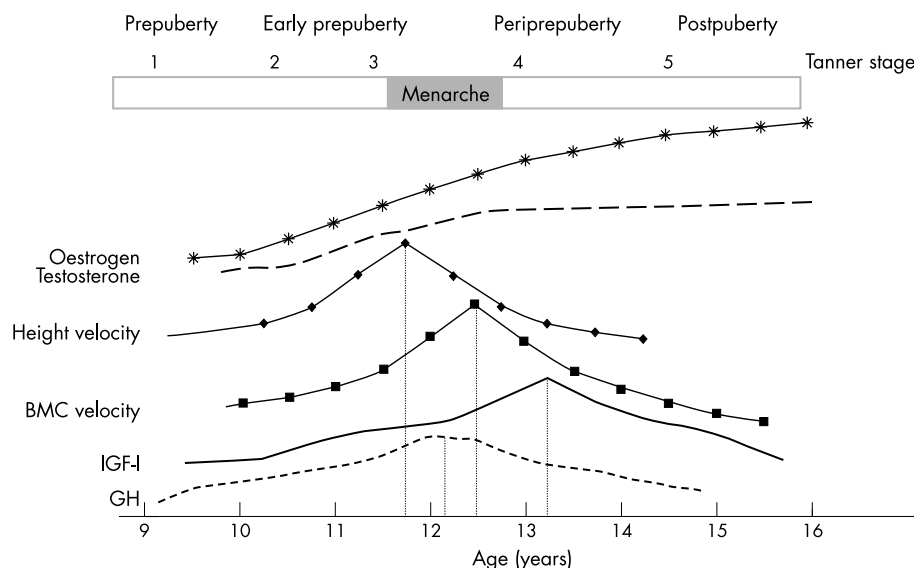


Figure 1 Peaks for height velocity, bone mineral content (BMC) velocity, growth hormone (GH) amplitude, and insulin-like growth factor-I (IGF-I) amplitude, and trends for oestrogen and testosterone levels in girls relative to average age and Tanner stage. Peaks (connected to age by dotted lines) for height velocity, BMC velocity, GH, and IGF-I show the average age/Tanner stage at which maximum gains in height or BMC are made, and when maximum levels of GH and IGF-I occur. In boys, peak height velocity and peak BMC velocity occur about 1.5 years later than in girls (at 13.4 years (Tanner stage 3) and 14.0 years (Tanner stage 4) respectively). Relations between peaks for height and bone velocities and peaks for GH and IGF-I are similar for boys and girls. Adapted from several references.<sup>14 18 19 25 43</sup>

around puberty and relate these to longitudinal change in linear growth and bone mineral gain. We then discuss how bone responds to exercise as measured by dual energy x ray absorptiometry (DEXA), based on published intervention studies in children and adolescents.

We performed a computerised literature search of the Medline database, covering the years 1966 to the present, using the keywords: intervention, training, exercise, children, boys, girls, adolescents, bone mineral. All relevant articles were retrieved, either locally or by interlibrary loan. The search was not limited to the English literature, and articles in all journals were considered. Fifty one articles were identified. Criteria for inclusion were: (a) exercise intervention study in a healthy cohort (non-clinical, non-athletes) with at least two measurement points; (b) subjects' age < 18 years; (c) areal bone mineral density (BMD) or bone mineral content (BMC) by DEXA as a primary outcome measure. Eight articles met all three criteria (table 1) and were reviewed.

#### STAGES OF MATURITY IN CHILDHOOD AND ADOLESCENCE

Chronological age does not adequately represent the diversity between children in the timing and intensity of the physiological changes that occur during growth.<sup>18</sup> Early and late maturing children of identical chronological age can differ by as much as six years developmentally.<sup>19</sup> Further, children at the same initial developmental stage may advance at vastly different rates.<sup>7</sup> Therefore, it is crucial that paediatric studies define the participants by both age and maturity.

There are a number of commonly used methods to assess a child's maturity. Skeletal age by standard radiography, although safe, is used rarely because it involves the use of ionising radiation. Tanner staging by self assessment, on the other hand, is non-invasive and has approximately the same degree of precision as assessing developmental age with hand-wrist radiographs.<sup>20 21</sup> Children classify themselves as Tanner stage 1–5 based on developmental diagrams of breasts (girls), pubic hair (for both girls and boys), and genitalia (boys).<sup>18</sup> Children in Tanner stage 1 are considered prepubertal, Tanner stages 2 and 3 represent the early pubertal phases, Tanner stage 4 adolescents are considered to be in the late stages of puberty,

whereas Tanner stage 5 represents full maturity, or the postpubertal adolescent.

There is a wide range of chronological ages within each Tanner stage. For example, in our study of early pubertal girls, Tanner stage 2 girls were 8.8–11.8 years old.<sup>22</sup> Tanner staging indicates the sequence of the events of puberty more aptly than does chronological age. In most girls, menarche is achieved after Tanner breast stage 3, and immediately after (about 7 months) peak height velocity. These events can occur any time between 10.5 and 15.5 years of age,<sup>18</sup> but are most commonly observed in girls at age 12.7 years (fig 1).<sup>14 23</sup> For the purposes of this review, "immature" and "mature" refer to the state of the reproductive system, with menarche in girls generally signalling maturational advancement (a fully "mature" girl or boy is Tanner stage 5).<sup>19</sup> Childhood is the period between infancy and the onset of puberty, and adolescence refers to the time after pubertal onset during which a mature reproductive system is attained.<sup>19</sup>

Finally, physical maturity in children may be assessed relative to peak height velocity, provided that a minimum of three years of longitudinal data have been collected. By this direct measurement method, a child can be identified along an individual growth continuum, whereas by Tanner staging, a child must be represented by one of five categories. On average, peak height velocity occurs at 11.7 years (Tanner stage 3) in girls and 13.4 (Tanner stage 4) years in boys.<sup>14 18</sup>

#### ENDOCRINE EVENTS IN MATURATION: THE BIOLOGICAL MECHANISMS OF CHANGE IN BONE

As we assume the reader is familiar with the various endocrine events in maturation, we briefly highlight the emerging influence of growth hormone (GH), insulin-like growth factor-I (IGF-I), and sex hormones on bone during this transition. Figure 1 illustrates the average changes in amplitude of these factors relative to maturational stage.

The peak amplitude of GH pulsatile secretion coincides with peak height velocity (fig 1),<sup>24 25</sup> and its influence on bone is probably mediated through insulin-like growth factors.<sup>26</sup> In prepubertal children, GH is the primary contributor to linear bone growth, whereas sex steroids act in concert with GH to exert a significant influence on bone during and beyond puberty.

Table 1 Skeletal loading exercise intervention studies in children and adolescents

Reference	Participants and design	Exercise intervention	Analytical approach	Results (% difference in gain between Ex and Con, after any statistical adjustments)
<i>Prepubertal</i> Bradney <i>et al</i> <sup>6</sup>	Boys. White. n=20 Con, n=20 Ex; mean age 10.4 (0.2); age range 8.4–11.8 years. All TS 1 throughout. Randomised by school: 1 Con + 1 Ex.	Programme: One PE teacher supervised intervention programme outside of school time. Included aerobics, soccer, volleyball, dance, gymnastics, basketball, weight training. Frequency & duration: 3 times/week; 30 minutes/session; 8 months duration. Progression: Not stated.	Con and Ex matched for age, standing height, sitting height, weight, baseline aBMD. Unpaired <i>t</i> tests to compare bone changes between groups.	†TB: +1.2% aBMD. LS: +2.8% aBMD. PF: Not measured. FN: Not measured. GT: Not measured. ‡Femoral Mid-shaft: +5.6% BMC; +5.6% aBMD, vBMD NS, +6.4% cortical thickness.
Fuchs <i>et al</i> <sup>4</sup>	Girls & Boys. White. n=44 Con; n=45 Ex; mean age 7.5 (0.2); age range 5.9–9.8 years. All TS 1 throughout. Children were randomised to Con or Ex within one elementary school.	Programme: Intervention took place outside of regular PE classes, supervised by research team. Each session: 100 two footed drop landings from 61 cm height on to a wooden floor. Mean (SD) ground reaction force for drop jumps from 61 cm height was 8.8 (0.9) times body weight. Frequency & duration: 3 times/week; 10 minutes jumping/session; 7 months. Progression: Week 1–4: Progressed from 50 jumps per session (no box), to 80 jumps per session (from box). Week 5–end : 100 jumps from 61 cm box.	One factor ANCOVA; baseline bone, change in height, change in weight, and age as covariates.	TB: Not measured. LS: +3.1% BMC; +2.0% aBMD. PF: Not reported. FN: +4.5% BMC; aBMD not significant. GT: Not reported.
McKay <i>et al</i> <sup>8</sup>	Girls & Boys. Asian & White. n=81 Con; n=63 Ex; mean age 8.9 (0.7) years; age range 6.9–10.2 years. Boys were TS 1 throughout; 89% of girls were TS1 and 11% were TS 2 at baseline; ~30% of girls were TS 2 by follow up. Randomised by school: 5 Con + 5 Ex.	Programme: School based; teachers chose activities from a variety of games, circuits, dances which incorporated jumping. 10 tuck jumps performed before PE class, and once in classroom each week. Frequency & duration: 3 times/week; 10–30 minutes/session; 8 months. Progression: As per fitness level of class; more challenging activities added as options after 3 months.	2 (Ex, Con) × 2 (Asian, White) × 2 (male, female) ANOVA to examine bone changes between groups. Hierarchical regression to examine effect of intervention when baseline bone, height change, lean mass change, general physical activity, calcium, sex, and ethnicity controlled.	TB: Not significant. LS: Not significant. PF: Not significant. FN: Not significant. GT: BMC not significant; +1.4% aBMD.
<i>Early pubertal</i> Morris <i>et al</i> <sup>1</sup>	Girls. Ethnicity not stated, schools matched for ethnicity. n=33 Con; n=38 Ex girls; mean age 9.5 (0.9) years; age range 9–10 years. All premenarcheal throughout; TS 1–3. Not randomised; schools self selected: 1 Con + 1 Ex.	Programme: One PE teacher supervised intervention programme outside of school time. Included aerobics, soccer, football, step aerobics, dance, skipping, ball games, weight training. Frequency & duration: 3 times/week; 30 minutes/session; 10 months. Progression: In 10 week weight training session only.	Independent <i>t</i> tests to compare bone change between groups. ANCOVA (with change in height and total body mass as covariates) to compare adjusted change in bone between groups.	TB: +5.5% BMC; +2.3% aBMD. LS: BMC not significant; +3.6% aBMD; +2.9% vBMD. PF: BMC not significant; +3.2% aBMD. FN: +4.5% BMC; aBMD not significant; vBMD not significant. GT: Not reported.
<i>Adolescents</i> Blimkie <i>et al</i> <sup>7</sup>	Girls. Ethnicity not stated. n=16 Con, n=16 Ex girls. Mean age 16.2 (0.2) years; age range 14–18 years. All postmenarcheal (TS 4–5) at baseline. Girls were randomised to Con or Ex within 1 highschool.	Programme: Resistance training using hydraulic machines (13 exercises, 4 sets with 10–12 reps of each). Sessions supervised by researchers. Frequency & duration: 3 times/week; session duration not stated; 6.5 months. Progression: Resistance increased every 6 weeks.	Con and Ex matched for age, body mass, level of habitual physical activity. Two way repeated measures ANOVA used to compare change in bone between groups.	TB: Not significant. LS: Not significant. PF: Not measured. FN: Not measured. GT: Not measured.

Table 1 Continued Skeletal loading exercise intervention studies in children and adolescents

Reference	Participants and design	Exercise intervention	Analytical approach	Results (% difference in gain between Ex and Con, after any statistical adjustments)
Witzke <i>et al</i> <sup>68</sup>	Girls. All white. n=29 Con; n=27 Ex; mean age 14.6 (0.5) years; age range 13–15 years. All postmenarcheal at baseline. Con and Ex matched for age and months postmenarche. Not randomised; exercisers participated for PE credit at 2 highschools.	Programme: First 3 months: resistance training + plyometrics. Next 6 months: plyometrics, including jumps, depth jumps, bounding and hopping on soft surfaces. Frequency & duration: 3 times/week; 30–45 minutes/session; 9 months. Progression: Weight training progressed from months 1–3: repetitions, sets, and weight gradually increased. Plyometric training progressed in jump difficulty and number of reps.	Repeated measures ANOVA.	TB: Not significant. LS: Not significant. PF: Not significant. FN: Not significant. GT: Not significant. ‡Femoral Mid-shaft: Not significant.
Two maturity groups Heinonen <i>et al</i> <sup>6</sup>	Girls. All white. n=58 (33 Con + 25 Ex) Premenarcheal (TS 1–3, mean age 11.0 (0.9) years (Con), 11.7 (1.3) years (Ex)). n=68 (29 Con + 39 Ex) Postmenarcheal (TS 2–5; mean age 13.7 (0.9) years (Con & Ex)). Not randomised; schools self-selected to 2 Ex + 3 Con.	Programme: Jump training sessions incorporating single and two foot jumps from floor, and on and off a 30 cm box. Frequency & duration: 2 times/week; 20 minutes jump training/session; 9 months. Progression: Progressed gradually from two foot floor jumps (100 jumps) to combination one and two foot jumps from box (200 jumps).	Individual BMC values normalised by the length of the ROI. ANCOVAs performed within each maturity group, (baseline bone values and age as covariates).	Premenarcheal: TB: Not measured. LS: +3.3% BMC. PF: Not significant. FN: +4.0% BMC. GT: Not significant. §Tibial Mid-shaft: Not significant. No significant differences between postmenarcheal Ex and Con.
MacKelvie <i>et al</i> <sup>6</sup>	Girls. Mixed ethnicities (primarily white + Asian). n=70 (26 Con + 44 Ex) Prepubertal (TS 1, mean age 10.1 (0.5) years). n=107 (64 Con + 43 Ex) Early pubertal (TS 2 + 3, mean age 10.5 (0.6) years). Randomised by school: 7 Ex + 7 Con.	Programme: School based, circuit training programme, integrated into physical education classes, supervised by classroom teachers. All station activities incorporated jumping activities: i.e., drop jumps, star jumps, lunge jumps, hopping, plyometric jumps, jumping over obstacles. Average ground reaction force for various jumps ranged between 3.5–5 times body weight. Frequency & duration: 3 times/week; 12 minutes/session; 7 months. Progression: Levels 1–3 (–2 ½ months at each level). Number of jumps increased within level (50–100); and jump difficulty/height increased between levels.	ANCOVAs within maturity categories to compare bone change between groups (controlling for age, maturity, baseline bone values, change in height and/or bone area).	No significant differences between prepubertal Ex and Con. Early pubertal: TB: Not significant. LS: +1.8% BMC; +1.7% aBMD. PF: Not significant. FN: +1.9% BMC; +1.6% aBMD; +3.1% vBMD. GT: Not significant.

Con, Controls; Ex, Exercisers; TS, Tanner Stage; ROI, region of interest; ANOVA, analysis of variance; ANCOVA, analysis of covariance; TB, Total body; LS, Lumbar spine; PF, Proximal femur; FN, Femoral neck; GT, Greater trochanter; BMC, bone mineral content (by dual energy x ray absorptiometry (DEXA)); aBMD, areal bone mineral density; vBMD, volumetric bone mineral density (estimated from DEXA).

†Calculated eight month change from reported % change/month.

‡Bradney *et al*<sup>6</sup> and Witzke *et al*<sup>68</sup> were the only two studies that measured and reported change at the femoral midshaft (DEXA).

§Heinonen *et al*<sup>6</sup> was the only study that measured and reported change at the tibial midshaft (pQCT).

The simultaneous, and possibly synergistically anabolic, rise in GH and IGF-I levels is unique to the pubertal growth period.<sup>27</sup> IGF-I levels increase abruptly around the Tanner stage 1–2 transition, with a peak occurring around Tanner stage 4–5, and declining quickly thereafter.<sup>28</sup> In one large cross sectional study of boys and girls, IGF-binding protein-1 decreased from prepuberty to peripuberty, with a slight rise noted after the age 17 years, indicating a higher level of free, biologically active IGF during puberty.<sup>28</sup>

“... a particularly opportune time to intervene with loading exercise is probably when free, biologically active IGF-I levels are climbing.”

Serum IGF levels are associated with bone mineral in early pubertal girls,<sup>29</sup> and cross sectional and cortical bone areas in 7–18 year old girls and boys.<sup>30</sup> An 18 month longitudinal study of Tanner stage 1 and 2 male gymnasts showed a strong correlation ( $r = 0.67$ ,  $p < 0.05$ ) between change in calcaneal ultrasound bone variables and baseline serum IGF-I.<sup>31</sup> Thus, the bone change resulting from extreme high impact activity may be mediated, or promoted, by high levels of IGF-I. Although exercise is recommended to maximise bone health at all stages of life, one can speculate that a particularly opportune time to intervene with loading exercise is when free, biologically active IGF-I levels are climbing (Tanner stages 2–4; fig 1).

With respect to sex hormones, in both girls and boys, oestrogens probably have greater influence on bone accrual,<sup>32</sup> bone turnover, linear growth,<sup>33</sup> apposition of bone on the endosteal surface,<sup>34</sup> and epiphyseal closure.<sup>35</sup> Androgens probably have stronger ties to cortical bone size.<sup>32–33</sup> In girls, oestrogen levels increase significantly between Tanner stages 2 and 4,<sup>36–37</sup> corresponding to the timing of peak bone velocity,<sup>14</sup> as well as menarche (fig 1).<sup>23</sup> The steepest slope of increase for testosterone in girls was noted between Tanner stages 2 and 3.<sup>36</sup> In maturing boys, the greatest absolute change in oestrogen occurred between Tanner stages 4 and 5,<sup>25</sup> corresponding to the timing of peak bone velocity.<sup>14</sup> A surge in testosterone follows Tanner stage 2.<sup>25–38</sup>

## BONE MINERAL ACCRUAL AND STAGES OF MATURITY

Through the concerted influences of growth and systemic hormones, bone mineral accrual is substantially altered between childhood and puberty. A six year longitudinal study in 53 girls and 60 boys (initially 8–14 years of age) showed an approximately one year lag between peak height velocity and peak bone velocity (12.5 years in girls and 14.1 years in boys) (fig 1).<sup>14</sup> Importantly, about 26% of final adult bone is accumulated during the two years surrounding peak bone velocity, which approximates the amount of bone lost during the postmenopausal years.<sup>7</sup> These two critical years correspond to ages 11.5–13.5 for girls (Tanner stages 2–4) and 13.05–15.05 in boys (Tanner stages 3–5).

The maturity related changes occurring at the endosteal and periosteal bone surfaces that may be influenced by exercise are reviewed elsewhere.<sup>26–34–40</sup> It is notable that aspects associated with growth culminate to offer greater potential for an osteogenic response when the mechanical loading environment is changed. Immature bone is capable of modelling, which is responsible for adaptations in bone size, shape, and content.<sup>41</sup> Also, there is substantial gain of cortical bone on both the periosteal and endocortical surfaces, which is unique to the pubertal growth spurt.<sup>42</sup>

## EXERCISE AND BONE MINERAL ACCRUAL IN CHILDREN AND ADOLESCENTS

Activity and bone change related to maturity  
Few intervention studies offer insight into the time during growth when bone responds optimally to physical loading.<sup>43</sup>

There is, however, a substantial body of research that supports the strong influence of high impact activities (gymnastics, triple jump, racquet sports, power lifting) on bone modelling changes in children.<sup>9–11 44–46</sup>

General levels of physical activity are positively related to both the magnitude and rate of bone mineral accrual during peak growth.<sup>14</sup> In the six year University of Saskatchewan bone mineral accrual study, active girls and boys accrued 10–40% more bone (depending on skeletal region) during the two years surrounding peak bone velocity than inactive children. However, this study provides no data on the relative rates of accrual between active and inactive children at different pubertal stages.

One cross sectional study investigated the relation between maturity and bone mineral in 91 female racquet sport players aged 7–17 and healthy, maturity matched counterparts.<sup>11</sup> Proximal humerus, humeral shaft, and distal radius side to side areal BMD differences were significantly greater in players than controls at Tanner stages 3, 4, and 5. There were no differences between Tanner stage 1 players and controls; Tanner stage 2 girls differed only at the humeral shaft, the most heavily loaded site. A limitation of this observational study was that training volumes also increased with Tanner stage and critics have suggested that this may have influenced greater bone gains in Tanner 3–5 girls, independently of maturity.<sup>47</sup> Haapasalo et al<sup>11</sup> showed that training time did not correlate with side to side areal BMD differences in the Tanner stage 1 or 2 players, whereas these variables correlated moderately in Tanner stage 3–5 players. Thus, frequent training was not significantly associated with bone gain in Tanner stages 1 and 2. The side to side areal BMD differences between peripubertal players and controls (about 10% at Tanner stage 3 and beyond) raise the possibility of a synergism between advancing pubertal status and loading induced bone gain. However, only prospective studies that intervene with similar amounts and intensities of activity across maturity levels can truly investigate the presence of a window of opportunity for peripubertal bone gain. The remainder of this systematic review is structured according to maturity status and focuses on intervention studies in children that met the inclusion criteria outlined above. Table 1 summarises the data.

## Exercise intervention studies in prepubertal children

There have been two exercise intervention studies in children who were classified as prepubertal at both baseline and after the intervention (table 1).<sup>2–4</sup> The difference in eight month bone mineral gain between intervention and control groups was 1.2–5.6% by BMC and/or areal BMD, depending on measurement site (table 1). With respect to bone structure,<sup>2</sup> cortical thickness increased more in intervention boys than controls. This change was due to greater endosteal apposition, not an increase in periosteal diameter.<sup>2</sup> Further work is needed to make the link between increases in BMC or areal BMD and increases in bone strength.

Although the response over eight months was similar between studies, the intervention programmes were distinct (table 1). One study prescribed a 30 minute, 3 times/week extracurricular weight-bearing exercise programme involving a range of games and activities.<sup>2</sup> The other implemented a highly intensive, repetitive, box jumping programme<sup>4</sup> (table 1). This elicited ground reaction forces of 9 times body weight, compared with typical paediatric ground reaction forces of 3 times body weight during running,<sup>48</sup> and 10 times body weight in elite gymnastics training.<sup>49</sup>

From these studies it appears that, for prepubertal children, the format or specificity of intervention may be less important than the magnitude of increase in weight-bearing activity. The activities in both interventions supplemented the regular two hours/week<sup>2</sup> and 30 minutes/week<sup>4</sup> physical education curricula. There were no differences in extracurricular physical



activity or sports participation between intervention and control groups in either study. Thus, the interventions represented substantial 75%<sup>2</sup> and 150%<sup>4</sup> increases respectively in weight-bearing activity compared with that undertaken by controls in their regular physical education classes and extracurricular activities.

These data show that the prepubertal skeleton is responsive to intense, aggressive exercise programmes that introduce a significant amount of mechanical loading, beyond that which is typically provided in physical education classes.<sup>2,4</sup> Bone mineral change and growth in prepuberty are largely influenced by GH, and occur independently of the input of sex steroids (unlike during early puberty and peripuberty). Acute bouts of intense exercise may activate the GH-IGF-I axis in both prepuberty<sup>50</sup> and peripuberty.<sup>37</sup> Long term activation and elevation of these hormones may mediate an effect on bone over time. Skeletal loading intervention studies have not thus far investigated the hormonal mechanisms underlying modelling changes in immature bones. It is unclear whether increases in GH are necessary to promote bone gain, and whether less vigorous programmes—ones that take less time, and incorporate a variety of moderate impact activities—could be effective in promoting bone mineral accrual in prepubertal children.

McKay et al<sup>3</sup> implemented a less vigorous, school based, bone loading programme, facilitated by the participants' regular classroom within the physical education curriculum. The group was largely (89%) prepubertal at baseline. During each physical education class, children performed games and circuits involving jumping or skipping, and did 10 tuck jumps<sup>3</sup> (table 1). The intervention did not require children to participate in any extra physical activity outside of school compared with that of children at control schools, and therefore the programme represented a change in activity type rather than an increase in duration. Changes in areal BMD at the trochanter were significantly greater (1.4%,  $p < 0.01$ ) in the intervention children. Other studies of prepubertal children did not measure<sup>2</sup> or did not report<sup>4</sup> change at the trochanter. The less vigorous nature of the school based intervention may explain the non-significant difference in change at other measured sites. As many of the activities involved running with jumping, muscle pull at the trochanter may have been substantial, resulting in greater change in this highly trabecular area.<sup>51,52</sup>

**Exercise intervention studies in early pubertal children**  
Using a similar intervention as Bradney et al<sup>2</sup> (table 1), Morris and colleagues investigated the bone response at several skeletal sites in a mixed group of prepubertal and early pubertal (all premenarcheal) girls.<sup>1</sup> After controlling for differences in change in height and weight, girls in the intervention group gained significantly more total body, lumbar spine, and proximal femur bone mineral (2.3–5.5%, depending on bone site and parameter; table 1) than controls. This study was the first to address exercise induced bone gain in immature girls, and the greater differences in bone mineral gain between intervention and control groups in this study compared with previous exercise studies in adults<sup>53–56</sup> highlighted the growing years as a potentially important time for intervention. Before menarche, oestrogen, GH, IGF-I, and testosterone levels reach higher levels (fig 1), all factors that enhance bone formation. In combination with accelerating growth velocity, bone modelling and remodelling may occur more readily under the influence of mechanical loading.

#### Exercise intervention studies in adolescents

Two exercise intervention studies in postmenarcheal girls failed to significantly increase bone mineral compared with the control groups.<sup>57,58</sup> In both studies, the intervention and control girls were well matched for maturational status, and

the exercise programmes involved substantial amounts of training. The first implemented a progressive, 6.5 month weight training programme, involving exercises on hydraulic machines targeting both the trunk and limbs.<sup>57</sup> Changes in lumbar spine bone variables did not differ significantly between intervention and control girls during the intervention. The use of hydraulic machines may not have created an optimal strain environment (in terms of impact and novel distributions)<sup>59</sup> to elicit changes in bone. However, the role of maturity becomes apparent when intervention girls failed to show greater changes in BMC than their maturity matched controls after completing a complex, high impact, intense, nine month, plyometric training programme<sup>58</sup> (table 1). As shown in fig 1, postmenarche (Tanner stages 4–5) corresponds to the descent of peaks for height and bone velocities, GH, and IGF-I. As these pivotal bone enhancing factors decrease, it probably becomes more difficult to promote modelling changes in bone. Furthermore, as has been shown in animal studies, the bone response to a given level of strain decreases with maturity.<sup>60,61</sup>

#### Exercise intervention studies in two distinct maturational groups

A recently published prospective intervention addressed the issue of maturity related skeletal responsiveness to mechanical loading by simultaneously intervening with an intense jumping programme (table 1) in premenarcheal ( $n = 25$ , Tanner stage 1–3) and postmenarcheal girls ( $n = 38$  Tanner stage 3–5,  $n = 1$  Tanner stage 2).<sup>5</sup> BMC changes at the lumbar spine and femoral neck were 3–4% greater in premenarcheal intervention girls than premenarcheal controls; changes did not differ by intervention and control groups in the postmenarcheal girls.

Premenarcheal exercisers tended to have greater, although not significant, gains in cortical cross sectional area (relating to a change in bone structure) and cortical density, at the tibial midshaft, as measured by peripheral quantitative computed tomography.<sup>5</sup> Changes in section modulus (an estimation of bone strength) at the tibial shaft did not differ significantly between groups. Peripheral quantitative computed tomography can be used in future studies to compare changes in both bone mass and structure between more highly trabecular areas—for example, distal tibia—and the highly cortical tibial midshaft.<sup>5</sup>

Heinonen et al<sup>5</sup> provided some evidence that the osteotrophic potential may be greater in the premenarcheal years compared with postmenarche. It is important to note that premenarche includes both prepubertal and early pubertal children, who, biologically have different mechanisms of bone change.

We recently intervened in prepubertal (Tanner stage 1) and early pubertal (Tanner stage 2 and 3) girls who took part in the same seven month, circuit training programme of jumping exercises within their physical education classes (table 1).<sup>6</sup> Early pubertal girls on this programme had greater bone change at the femoral neck and lumbar spine than maturity matched controls. Analysing these data using the hip structural analysis programme<sup>62</sup> elucidated the structural changes that underpin the bone mass gains in the early pubertal intervention girls.<sup>40</sup> These girls had a greater change in femoral neck bone cross sectional area and reduced endosteal expansion, accompanied by a greater improvement in section modulus (bending strength) than controls. The bone mineral<sup>6</sup> and structural<sup>40</sup> changes in the prepubertal intervention girls did not differ at any site from those of their prepubertal controls (table 1). Taken together, results from these studies<sup>5,6,40</sup> may indicate that bone mass and structure are particularly responsive to certain exercise prescriptions during the earliest onset of puberty in girls, corresponding, on average, to ages 10–12 years. In boys, the corresponding

## Take home message

During the very early stages of puberty, bone may be particularly responsive to weight-bearing, high impact exercise, attainable in a range of youth sports and activities or in brief sessions of jumping activity.

maturational stage would be 12–14 years, but studies in prepubertal, peripubertal, and postpubertal boys are needed to substantiate this.

## EXERCISE DURING CHILDHOOD AND BONE IN LATER LIFE

To qualify as a legitimate long term prescription for bone health in adulthood and later life, the effects on bone of exercise during childhood must persist so that fracture is prevented. Whether gains in bone mineral and bone strength from exercise in childhood reduce fracture risk in later life is a controversial issue—the “Achilles heel of exercise”.<sup>63–65</sup> Currently, there is very little research to support either side of the argument, as follow up studies are rare. In a five year follow up study, previously elite, retired racquet sport athletes maintained higher bone mineral, even with greatly reduced training, compared with controls of similar age.<sup>12</sup> Two retrospective studies in previously elite, retired ballet dancers<sup>13</sup> and gymnasts<sup>10</sup> provide evidence of a persistence of a bone mineral advantage over controls. Follow up studies of exercise interventions in children have yet to be conducted and published. However, in women, six months of detraining diminished the positive effects on bone apparent after a 12 month resistance training programme,<sup>66</sup> and a cross sectional study of retired male soccer players indicated that, after 35 years of retirement, areal BMD was similar between the former athletes and controls.<sup>67</sup>

Further work linking childhood exercise to bone health in later life is critical. Future studies need to incorporate diverse measures, such as magnetic resonance imaging and peripheral computed quantitative tomography at several bone regions, to adequately approximate the full impact of an intervention in an immature population. There is a need for a controlled exercise intervention that tests the magnitude of skeletal effects separately across all stages of maturation to fully assess the existence of a window of opportunity when the skeletal response to loading exercise is at a maximum. At this point, the best recommendation is to encourage loading exercise during growth, which will ideally foster the maintenance of an active lifestyle and promote bone health over one's lifetime.

The clinician can play an active role to help ensure the attainment of a healthy peak bone mass by discussing with young patients and their parents the importance of an active lifestyle for bone mineral gain during growth. In a *Journal of Pediatrics* editorial, Stanford paediatrician, Laura Bachrach emphasised, “the time has come . . . to recognise the importance of (childhood) exercise as an essential component of osteoporosis prevention.”<sup>68</sup>

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## REFERENCES

- Morris FL, Naughton GA, Gibbs JL, *et al.* Prospective 10-month exercise intervention in pre-menarcheal girls: positive effects on bone and lean mass. *J Bone Miner Res* 1997;12:1453–62.
- Bradney M, Pearce G, Naughton G, *et al.* Moderate exercise during growth in prepubertal boys: changes in bone mass, size, volumetric density, and bone strength: a controlled prospective study. *J Bone Miner Res* 1998;13:1814–21.
- McKay HA, Petit MA, Schutz RW, *et al.* Augmented trochanteric bone mineral density after modified physical education classes: a randomized school-based exercise intervention study in pre- and early-pubescent children. *J Pediatr* 2000;136:156–62.
- Fuchs RK, Bauer JJ, Snow CM. Jumping improves hip and lumbar spine bone mass in prepubescent children: a randomized controlled trial. *J Bone Miner Res* 2001;16:148–56.
- Heinonen A, Sievanen H, Kannus P, *et al.* High-impact exercise and bones of growing girls: a 9-month controlled trial. *Osteoporosis Int* 2000;11:1010–17.
- MacKelvie KJ, McKay HA, Khan KM, *et al.* A school-based loading intervention augments bone mineral accrual in early pubertal girls. *J Pediatr* 2001;139:501–8.
- Bailey DA. The Saskatchewan Pediatric Bone Mineral Accrual Study: bone mineral acquisition during the growing years. *Int J Sports Med* 1997;18:S191–4.
- Kannus P, Niemi S, Parkkari J, *et al.* Hip fractures in Finland between 1970 and 1997 and predictions for the future. *Lancet* 1999;353:802–5.
- Virvidakis K, Georgiou E, Korkotsidis A, *et al.* Bone mineral content of junior competitive weightlifters. *Int J Sports Med* 1990;11:244–6.
- Bass S, Pearce G, Bradney M, *et al.* Exercise before puberty may confer residual benefits in bone density in adulthood: studies in active prepubertal and retired female gymnasts. *J Bone Miner Res* 1998;13:500–7.
- Haapasalo H, Kannus P, Sievanen H, *et al.* Effect of long-term unilateral activity on bone mineral density of female junior tennis players. *J Bone Miner Res* 1998;13:310–19.
- Kontulainen S, Kannus P, Haapasalo H, *et al.* Good maintenance of exercise-induced bone gain with decreased training of female tennis and squash players: a prospective 5-year follow-up study of young and old starters and controls. *J Bone Miner Res* 2001;16:195–201.
- Khan KM, Bennell KL, Hopper JL, *et al.* Self-reported ballet classes undertaken between 10 and 12 years of age and hip bone mineral density. *Osteoporosis Int* 1998;8:165–73.
- Bailey DA, McKay HA, Mirwald RL, *et al.* A six year longitudinal study of the relationship of physical activity to bone mineral accrual in growing children: The University of Saskatchewan Bone Mineral Accrual Study. *J Bone Miner Res* 1999;14:1672–9.
- Siemenda CW, Reister TK, Hui SL, *et al.* Influences on skeletal mineralization in children and adolescents: evidence for varying effects of sexual maturation and physical activity. *J Pediatr* 1994;125:201–7.
- Walton J, Hoerr S, Heine L, *et al.* Physical activity and stages of change in fifth and sixth graders. *J Sch Health* 1999;69:285–9.
- Allison KR, Adlaf EM. Structured opportunities for student physical activity in Ontario elementary and secondary schools. *Can J Public Health* 2000;91:371–5.
- Tanner JM. *Foetus into man*. Cambridge: Harvard Press, 1978.
- Malina RM, Bouchard C. *Growth maturation and physical activity*. Champaign, IL: Human Kinetics Publishers, 1991.
- Mahmoodi S, Sharif BS, Chester EG, *et al.* Skeletal growth estimation using radiographic image processing and analysis. *IEEE Trans Inf Technol Biomed* 2000;4:292–7.
- Duke PM, Litt IF, Gross RT. Adolescents' self-assessment of sexual maturation. *Pediatrics* 1980;66:918–20.
- MacKelvie KJ, McKay HA, Khan KM, *et al.* Lifestyle risk factors for osteoporosis in Asian and Caucasian girls. *Med Sci Sports Exerc* 2001;33:1818–24.
- McKay HA, Bailey DA, Mirwald RL, *et al.* Peak bone mineral accrual and age of menarche in adolescent girls: a six-year longitudinal study. *J Pediatr* 1998;133:682–7.
- Brook CGD, Hindmarsh PC. The somatotrophic axis in puberty. *Endocrinol Metab Clin North Am* 1992;21:767–82.
- Klein KO, Martha PM, Blizzard RM, *et al.* A longitudinal assessment of hormonal and physical alterations during normal puberty in boys II. Estrogen levels as determined by an ultrasensitive bioassay. *J Clin Endocrinol Metab* 1996;81:3203–7.
- Parfitt AM. The two faces of growth: benefits and risks to bone integrity. *Osteoporosis Int* 1994;4:382–98.
- Mauras N, Rogol A, Haymond M, *et al.* Sex steroids, growth hormone, insulin-like growth factor-1: Neuroendocrine and metabolic regulation in puberty. *Horm Res* 1996;45:74–80.
- Juul A, Dalgaard P, Werner F, *et al.* Serum levels of insulin-like growth factor (IGF)-binding protein-3 (IGFBP-3) in healthy infants, children and adolescents: the relation to IGF-1, IGF-II, IGFBP-1, IGFBP-2, age, sex, body mass index, and pubertal maturation. *J Clin Endocrinol Metab* 1995;80:2534–42.
- Libanati C, Baylink DJ, Lois-Wenzel E, *et al.* Studies on the potential mediators of skeletal changes occurring during puberty in girls. *J Clin Endocrinol Metab* 1999;84:2807–14.
- Mora S, Pitukcheewanont P, Nelson JC, *et al.* Serum levels of insulin-like growth factor I and the density, volume, and cross-sectional area of cortical bone in children. *J Clin Endocrinol Metab* 1999;84:2780–3.
- Daly RM, Rich PA, Klein R. Influence of high impact loading on ultrasound bone measurements in children: a cross-sectional report. *Calcif Tissue Int* 1997;60:401–4.
- Grumbach M. Estrogen, bone, growth and sex: a sea change in conventional wisdom. *J Pediatr Endocrinol Metab* 2000;13:1439–55.
- Geusens P, Cantatore F, Nijs J, *et al.* Heterogeneity of growth of bone in children at the spine, radius and total skeleton. *Growth Dev Aging* 1991;55:249–56.

- 34 Seeman E. From density to structure: growing up and old on the surfaces of bone. *J Bone Miner Res* 1997;12:509–21.
- 35 Cutler GBJ. The role of estrogen in bone growth and maturation during childhood and adolescence. *J Steroid Biochem Mol Biol* 1997;61:141–4.
- 36 Lee PA, Xenakis T, Winer J, *et al.* Puberty in girls: correlation of serum levels of gonadotropins, prolactin, androgens, estrogens, and progestins with physical changes. *J Clin Endocrinol Metab* 1976;43:775–84.
- 37 Laaneots L, Karelson K, Smirnova T, *et al.* Hormonal responses to exercise in girls during sexual maturation. *J Physiol Pharmacol* 1998;49:121–33.
- 38 Lee PA, Migeon CJ. Puberty in boys: correlation of plasma levels of gonadotropins (LH, FSH), androgens (testosterone, androstenedione, dehydroepiandrosterone and its sulfate), estrogens (estrone and estradiol) and progestins (progesterone and 17-hydroxyprogesterone). *J Clin Endocrinol Metab* 1975;41:556–62.
- 39 Reference withdrawn.
- 40 Petit MA, McKay HA, MacKelvie KJ, *et al.* A randomized school-based jumping intervention confers site and maturity-specific benefits on bone structural properties in girls: a hip structural analysis study. *J Bone Miner Res* 2002;17:363–72.
- 41 Barr SI, McKay HA. Nutrition, exercise and bone status in youth. *Int J Sport Nutr* 1998;8:124–42.
- 42 Garn SM. The course of bone gain and the phases of bone loss. *Orthop Clin North Am* 1972;3:503–20.
- 43 Khan KM, McKay HA, Haapasalo H, *et al.* Does childhood and adolescence provide a unique opportunity for exercise to strengthen the skeleton? *J Sci Med Sport* 2000;3:150–64.
- 44 Courteix D, Lespessailles E, Peres SL, *et al.* Effect of physical training on bone mineral density in prepubertal girls: a comparative study between impact-loading and non-impact-loading sports. *Osteoporosis Int* 1998;8:152–8.
- 45 Grimston SK, Wilows ND, Hanley DA. Mechanical loading regime and its relationship to bone mineral density in children. *Med Sci Sports Exerc* 1993;25:1203–10.
- 46 Nordstrom P, Pettersson U, Lorentzon R. Type of physical activity, muscle strength, and pubertal stage as determinants of bone mineral density and bone area in adolescent boys. *J Bone Miner Res* 1998;13:1141–8.
- 47 Bass SL. The prepubertal years: a uniquely opportune stage of growth when the skeleton is most responsive to exercise? *Sports Med* 2000;30:73–8.
- 48 Engsberg JR, Lee AG, Patterson JL, *et al.* External loading comparisons between able-bodied and below-knee-amputee children during walking. *Arch Phys Med Rehabil* 1991;72:657–61.
- 49 Daly RM, Rich PA, Klein R, *et al.* Effects of high-impact exercise on ultrasonic and biochemical indices of skeletal status: a prospective study in young male gymnasts. *J Bone Miner Res* 1999;14:1222–30.
- 50 Eliakim A, Scheett TP, Newcomb R, *et al.* Fitness, training, and the growth hormone-insulin-like growth factor 1 axis in prepubertal girls. *J Clin Endocrinol Metab* 2001;86:2797–802.
- 51 Singleton MC, LeVeau BF. The hip joint: structure, stability and stress. *Phys Ther* 1975;55:957–73.
- 52 Bobbert MF, Huijing PA, van Ingen Scheanau GJ. Drop jumping I: the influence of jumping technique on the biomechanics of jumping. *Med Sci Sports Exerc* 1984;4:332–8.
- 53 Heinonen A, Kannus P, Sievanen H, *et al.* Randomised controlled trial of effect of high-impact exercise on selected risk factors for osteoporotic fractures. *Lancet* 1996;348:1343–7.
- 54 Blumenthal JA, Emery CF, Madden DJ, *et al.* Effects of exercise training on bone density in older men and women. *J Am Geriatr Soc* 1991;39:1065–70.
- 55 Bravo G, Gauthier P, Roy PM, *et al.* Impact of a 12-month exercise program on the physical and psychological health of osteopenic women. *J Am Geriatr Soc* 1996;44:756–62.
- 56 Snow-Harter C, Bouxsein M, Lewis B, *et al.* Effects of resistance and endurance exercise on bone mineral status of young women: a randomized exercise intervention trial. *J Bone Miner Res* 1992;7:761–9.
- 57 Blimkie C, Rice S, Webber C, *et al.* Effects of resistance training on bone mineral content and density in adolescent females. *Can J Physiol Pharmacol* 1996;74:1025–33.
- 58 Witzke KA, Snow CM. Effects of plyometric jump training on bone mass in adolescent girls. *Med Sci Sport Exerc* 2000;32:1051–7.
- 59 Skerry T. Mechanical loading and bone: what sort of exercise is beneficial to the skeleton? *Bone* 1997;20:179–81.
- 60 Turner CH, Takano Y, Owan I. Aging changes mechanical loading thresholds for bone formation in rats. *J Bone Miner Res* 1995;10:1544–9.
- 61 Steinberg ME, Trueta J. Effects of activity on bone growth and development in the rat. *Clin Orthop* 1981;156:52–60.
- 62 Beck TJ, Ruff CB, Warden KE, *et al.* Predicting femoral neck strength from bone mineral data: a structural approach. *Invest Radiol* 1990;25:6–18.
- 63 Sievanen H, McKay H, Heinonen A, *et al.* The Achilles heel of exercise [letter; comment]. *Lancet* 2000;355:1909, discussion 1911.
- 64 Seeman E. The achilles heel of exercise-induced bone mass increments: cessation of exercise. *J Bone Miner Res* 2001;16:1370–1.
- 65 Kontulainen S, Kannus P. Cessation of treatment: a universal achilles' heel. *J Bone Miner Res* 2001;16:1372–3.
- 66 Winters KM, Snow CM. Detraining reverses positive effects of exercise on the musculoskeletal system in premenopausal women. *J Bone Miner Res* 2000;15:2495–503.
- 67 Karlsson MK, Linden C, Karlsson C, *et al.* Exercise during growth and bone mineral density and fractures in old age. *Lancet* 2000;355:469–70.
- 68 Bachrach L. Making an impact on pediatric bone health. *J Pediatr* 2000;136:137–8.

## COMMENTARY

The authors examined the important issue of whether there is a critical window of opportunity when bone is most responsive to exercise in children. In the first part, the stages of maturity in childhood and adolescence in relation to hormone amplitudes and height and bone velocities were reviewed. There is a wide range in a child's maturity for any given chronological age; therefore it is crucial that a child's maturity be assessed. Tanner staging by self assessment was presented as a non-invasive method that has a similar degree of precision as standard radiographs. For longitudinal studies, peak height velocity could also be used to assess physical maturity. About one quarter of adult bone is accumulated in the two years surrounding peak bone mineral content velocity, which corresponds to ages 11.5–13.5 years for girls (Tanner stages 2–4) and 13–15 in boys (Tanner stages 3–5). Secondly, the authors reviewed exercise intervention studies in children to determine if there is evidence for a critical period of bone accrual in children and adolescents. An increase in bone mineral has been found in exercise interventions in children; however, more research is needed to determine the long term effects of these gains. Finally, the authors speculate on preliminary findings that a window of opportunity for bone response may exist in early puberty.

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